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The prevalence of myopia and high myopia, and the association with education: Shanghai Child and Adolescent Large-scale Eye Study (SCALE)

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Complete List of Authors:	He, Xiangui; Shanghai Eye Disease Prevention and Treatment Center, Preventative Ophthalmology Sankaridurg, Padmaja; Brien Holden Vision Institute Xiong, Shuyu; Shanghai Eye Disease Prevention and Treatment Center, Preventative Ophthalmology Li, Wayne; Brien Holden Vision Institute Naduvilath, Thomas Lin, Senlin; Shanghai Eye Disease Prevention and Treatment Center, Preventative Ophthalmology Weng, Rebecca Lv, Minzhi; Shanghai Eye Disease Prevention and Treatment Center, Preventative Ophthalmology Ma, Yingyan; Shanghai Eye Disease Prevention and Treatment Center, Preventative Ophthalmology Lu, Lina; Shanghai Eye Disease Prevention and Treatment Center, Preventative Ophthalmology Wang, Jingjing; Shanghai Eye Disease Prevention and Treatment Center, Preventative Ophthalmology Zhao, Rong; Shanghai Eye Disease Prevention and Treatment Center, Preventative Ophthalmology Resnikoff, Serge; Brien Holden Vision Institute, Zhu, Jianfeng; Shanghai Eye Disease Prevention and Treatment Center, Preventative Ophthalmology Zou, Haidong; Shanghai Eye Disease Prevention and Treatment Center, Preventative Ophthalmology Xu, Xun; Shanghai Eye Disease Prevention and Treatment Center, Preventative Ophthalmology
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The prevalence of myopia and high myopia, and the association with education: Shanghai Child and Adolescent Large-scale Eye Study (SCALE)

Running title: high myopia and education

Xiangui He[1,2] PhD, Padmaja Sankaridurg[3,4] PhD, Shuyu Xiong[2] PhD, Wayne Li[3,4] MD, Thomas Naduvilath[3,4] PhD, Senlin Lin[1] MSc, Rebecca Weng[3,4] GD, Minzhi Lv[1] MPH, Yingyan Ma[2] PhD, Lina Lu[1] MPH, Jingjing Wang[1] MPH, Rong Zhao[1] JM, Serge Resnikoff[3,4] PhD, Jianfeng Zhu[1]* MD, Haidong Zou [1,2]* MD, Xun Xu[1,2]* MD

Xiangui He and Padmaja Sankaridurg are equal first authors.

1. Department of Preventative Ophthalmology, Shanghai Eye Disease Prevention and Treatment Center, Shanghai Eye Hospital, Shanghai, China
2. Department of Ophthalmology, Shanghai Key Laboratory of Ocular Fundus Disease, Shanghai General Hospital, Shanghai Engineering Center for Visual Science and Photomedicine, Shanghai Jiao Tong University, Shanghai, China； National Clinical Research Center for Eye Diseases, Shanghai, China.
3. Brien Holden Vision Institute, Sydney, New South Wales, Australia
4. School of Optometry and Vision Science, University of New South Wales, Sydney, New South Wales, Australia

Corresponding:

Xun Xu, Email: drxuxun@sjtu.edu.cn

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Haidong Zou，Email: zouhaidong@sjtu.edu.cn

Jianfeng Zhu，Email: jfzhu1974@hotmail.com

Address: No. 380 Kangding Road, Shanghai, 200040, China； Telephone: +86 021-62539696

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Abstract

Objectives: To report on: a) overall and geographical variation in myopia and high myopia prevalence, and b) the impact of education on the spherical equivalent refractive error in children across Shanghai.

Design: Cross-sectional study.

Setting: Across all 17 districts of Shanghai.

Participants: 910,245 children aged 4 to14 years from a school-based survey conducted between 2012 and 2013.

Main outcome measures: Data of children with non-cycloplegic auto refraction, visual acuity assessment and questionnaire were analyzed (67%, n=606,476). Prevalence of myopia (≤-1.0D) and high myopia (≤-5.0D) was determined. We used a regression discontinuity design to determine the impact of school entry cut-off date (1 September) by comparing refractive errors at each age, for children born pre-September to post 1-September, and performed a multivariate analysis to explore risk factors associated with myopia. Data analysis was performed in 2017-2018.

Results: Prevalence of myopia and high myopia was 32.9% (95% CI:32.8-33.1) and 4.2% (95% CI:4.1-4.2) respectively. From 6 years of age onwards, children born pre-September were more myopic compared to those born post 1 September (ahead in school by one year, discontinuity at 6 yrs:-0.19D (95% CI: -0.09 to-0.30D);14 yrs:-0.67D (95% CI: -0.21 to-1.14D)).

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Conclusions: Our findings suggest that myopia is associated with education, that is primarily focused on near based activities. Efforts to reduce the burden should be directed to public awareness, reform of education and health systems.

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Strengths and limitations of this study

1. The large sample size across the various districts and ages presents us with an opportunity to determine disparities in prevalence within a region.

2. For the first time, we described the use of regression discontinuity model to better understand the effect of education on myopia and refractive error.

3. Prevalence was determined with non-cycloplegic autorefraction that tends to overestimate the myopia prevalence especially in younger children.

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Introduction

The intractable and escalating rise in the prevalence of myopia is fueling a public health crisis worldwide. In many East and South East Asian countries, including certain parts of China, the prevalence is nearly 80% among children aged 17-18 years. Although the prevalence differs geographically, myopia is prevalent and rising in many other parts of the world, including North America, Australia, Europe and Middle East.[1-4] For 2015 alone, the global burden related to myopia was estimated at US244 billion.[5] Most alarmingly, the recent decades have seen a trend with myopia presenting at younger ages than before and consequently, there is a higher overall risk of the individual eye reaching high myopia.[1 4] In younger individuals, high myopia increases the risk of retinal breaks and retinal detachment, whereas in older individuals, there is an increased risk for a myriad of complications such as glaucoma, cataract, and myopic maculopathy. Indeed, myopic maculopathy is already one of the leading causes of low vision and blindness among working adults in China and South East Asian region.[6 7]

It is well known that environmental factors such as time outdoors, socio-economic status, and urban location are significant risk factors for myopia and high myopia. Although a number of studies reported an association between education and myopia,[8-11] there is lack of direct evidence that schooling results in a more myopic refractive error in younger school-aged children, as well as the impact of early education, including education in kindergarten and primary school, which would be more important for myopia prevention in children. There is a need to better understand the influence of education as they aid in developing interventions to better address the growing burden of myopia.

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The Shanghai Child and Adolescent Large Eye Study is a large-scale, prospective, school-based survey undertaken across all 17 districts of Shanghai that provides the prevalence estimates for 606,476 children aged 4 to 14 years. In this article we present the overall prevalence of myopia, report the prevalence across the districts and determine the effect of schooling on refractive error.

Materials and methods

Study Overview

Detailed methods of the study were previously reported [12]. Briefly at the first visit undertaken in 2012 to 2013, it was aimed to screen all children aged 4 to14 years, from kindergarten to junior high, from all the 17 districts and counties of Shanghai, China. All schools and kindergartens, including the school for blind and vision impaired children were involved in the study. The Institutional Ethics Committee of Shanghai General Hospital, Shanghai Jiaotong University approved the protocol (ID: 2015KY149) and the study followed the tenets of the Declaration of Helsinki for experimentation on humans. Written consent was obtained from each participant.

Data Collection

For each participant, both unaided and presenting (i.e. with a corrective device if worn) visual acuity (VA) was measured and parents/carers were required to fill in a simple questionnaire in consultation with the child. The questionnaire was designed to elicit known risk factors and behavioral patterns of the child [12]. Distance VA was measured using a standard logarithmic visual acuity E chart (National Standard of People's Republic of China, GB 11533-1989) mounted on an illuminated cabinet with a

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luminance of 80-320 cd/m^2. Refraction was conducted using either the Topcon KR-8900 (Tokyo, Japan), Nidek AR-330A (Nagoya, Japan) or HUVITZ HRK-7000A (Gemjeong-dong, South Korea) auto refractors. Measurements taken with these auto refractors were found comparable [13]. The procedure adopted for quality control was previously presented [12].

Definitions

VA in the better eye was used and the prevalence of vision impairment (VI) was calculated based both uncorrected and presenting VA. Definitions for VI were in accordance with WHO criteria: no VI defined as 6/12 or better, mild VI as worse than 6/12 to 6/18 inclusive, moderate VI as worse than 6/18 to 6/60 inclusive, severe as worse than 6/60 to 3/60 inclusive, and blindness defined as worse than 3/60 [14].

Prevalence of myopia and high myopia was determined using spherical equivalent refractive error (SE) based on non-cycloplegic autorefraction. Myopia and high myopia were defined as SE of ≤ -1.0D and ≤ -5.0D in either eye respectively. To enable comparisons with previously published data, we also determined the prevalence of high myopia wherein SE was ≤ -6.00D. Since non-cycloplegic refraction overestimates myopia we applied an equation to correct for the overestimation, with the equation based on data gathered from a subset of 6017 children from Shanghai of similar ages whose refractive errors were measured using both non-cycloplegia and cycloplegia. The model used non-cycloplegic refractive error, age and uncorrected VA to arrive at the equation [15]:

Equation 1

$$y = 0.831 + (0.954 \times \text{non cycloplegic SE}) + (-0.065 \times \text{age}) + (0.539 \times \text{UCVA})$$

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$R^2 = 0.91$, (Eq, 1, where y = cycloplegic SE)

This adjustment provided an improved and conservative estimate of the myopia prevalence rather than that based on non-cycloplegic refraction alone.

Statistical Analysis

Prevalence of myopia and high myopia was determined by age, gender and district and were adjusted using equation 1 and further standardized to the age-gender distribution of all eligible children (1.19 million) in Shanghai. The 95% confidence limits were based on Wilson Score method [16]. The data for the 145 blind/vision impaired children was included in the vision impairment assessment but not for analysis related to prevalence of myopia and high myopia.

Association of demographic and behavioral factors with myopia and high myopia was explored using univariate and multivariate analysis with factors at $p<0.05$ included in the multivariate analysis. Model was developed using logistic regression and standard errors adjusted using robust estimation of variance for the clustering effects within each school. Steps included backward elimination followed by forward entry until only significant factors remained and strength of association was described using odds ratio (OR) and 95% CI. Area under ROC curve was the indicator for model discrimination. Statistical significance was set at 0.01.

The interrelationship between age, education and refractive error was evaluated using a regression discontinuity model. In the regression discontinuity model, children born in a given year were assigned to pre-September and post-1September groups based on the school start date i.e. 1 September as those born pre-September are in a higher class/grade compared to those born post or on

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1 September. The causal effect of the cut off value, i.e. the school start date on the refractive error was analysed. The aim was to determine if children born pre- September had a more myopic refractive error compared to those born post-September within the same year as the latter were in a lower school year.

Data cleaning and analysis were performed using SAS 9.3 (SAS Institute, Cary, NC, USA) and R3.2.0 (Vienna, Austria) in 2017-2018.

Patient and public involvement

Participants and the public were not involved in the design or planning of the study. The study had no patient advisers. Participants were not involved in recruiting other participants or conduct of the study. The study results are not planned to be disseminated to the participants.

Results

Study Population

Of the 1,196,763 eligible children in Shanghai during the study period, a total of 910,245 children, with a mean age of 9.0 ± 2.8 yrs, and a male-female ratio of 53.3:46.7 were enrolled. A total of 2002 schools (average of 452 children per school) participated and the distribution of the population across the ages was previously presented [12]. Of the data for the 910,245 children, only data from 606,476 children (66.6%) was complete with both visual acuity and non-cycloplegic refraction data. The mean age of these children was 9.1 ± 2.8 yrs and gender distribution was 53.3:46.7 for males versus females and was comparable to the larger sample of 910,245 children.

Prevalence of Myopia and High Myopia

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The overall adjusted and standardized prevalence of myopia was 32.9% (95% CI: 32.8-33.1).

The adjusted mean SE was -0.57 ± 1.99D (range: -22.4 to +15.5D). Table 1 presents the age and gender wise distribution of adjusted myopia prevalence and shows that prevalence increased with age with nearly 50% of 11-year-olds having myopia. Slightly greater prevalence was observed in females ($p < 0.001$).

The adjusted prevalence of high myopia (≤-5.00D) was 4.2% (95% CI: 4.1-4.2). Prevalence of high myopia was low until age 8 (<1%) and increased in prevalence thereafter to approximately 10% or more from age 13 and reached 15.2% in 14-year-olds. When using a higher cut-off criteria of ≤-6.00D, the adjusted prevalence fell to 2.1% (95% CI: 2.0-2.1). With the higher cut-off threshold, high myopia was observed in less than 1% of the cohort until age 9 and thereafter, increased steadily reaching a prevalence of 8.1% in 14-year-olds.

Considering uncorrected VA, of the 606,476 children, 92,413 (15.3% of entire sample) had VA ≤ 6/12 which was mostly due to myopia (86,243 eyes, 14.2% of entire sample). Similarly, when presenting VA was considered, 39,076/606,476 (6.4% of entire sample) had VA ≤ 6/12 of which 34,298 or 5.7% of entire sample were myopic (Table 2).

Risk Factors Associated with Myopia and High Myopia

Age was the most significant predictive factor for both myopia and high myopia. Compared to a child aged 4-6 years, at 9 years, the odds ratio of having myopia increased by 5 times and to 50 times at 14 years of age (OR=50.9, 95% CI: 46.6-55.7; p<0.0001) (Appendix Table 1). Similarly, for high myopia, compared to a child aged 4-6 years, at 9 years of age, the odds ratio for high myopia was 3

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times greater and was 44 times greater at 14 years of age (OR=44.1, 38.6-50.3; p<0.0001) (Appendix Table 2).

Of the other risk factors, females had a 20% greater risk of being myopic and highly myopic (for both myopia and high myopia: OR=1.2, 1.1-1.2, p<0.0001). Moreover, having either one or both parents myopic increased the odds of myopia in children by 1.6 and 2.2 times compared to children with no myopic parent. A similar trend but slightly higher odds was observed for high myopia, where children with one or both myopic parents having a higher risk by 1.7 and 2.6 times.

Behavioral factors such as holding a book too close while reading increased the odds for myopia by 20 to 50% and watching television at close distances increased the odds by 10 to 40%. Interestingly, having a rest after continuous was protective by 3 to 20% and time playing and in entertainment was also mildly protective (10%). The increase or decrease in odds were similar for both myopia and high myopia suggesting that the behavioral factors experienced and found influencing prevalence were the same.

Additionally, children born post 1September in a calendar year had a 18 to 23% lower risk of being myopic compared to those born pre-September.

Estimating the effect of School start date on SE refractive error

Figure 1 shows the effect of school start date in September on SE refractive error. Considering the case of 6-year-olds, it is seen that those that born pre- September (corresponding to the vertical grid line) were in 1st grade of primary school and had a more myopic SE whereas those born post-September were in Upper Kindergarten and had a less myopic refractive error. Overall, as children

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progressed through the school years (or grades) refractive error became more myopic and importantly, the myopic shift in refractive error at the September cut-off point became more pronounced with older children having a significant discontinuity or a much greater difference in refractive error at the 1 September cut-off date.

Figure 2 summarizes the difference in refractive error for those born pre-September compared to post 1 September. Those born before September 1 had a more myopic refractive error by approximately 0.2D at 6 years of age and this difference increased steadily with age and reached approximately 0.5D at 13 years of age and nearly 0.7 D at 14 years of age.

Using data gathered from the questionnaire, it was seen that during the kindergarten years, time spent outdoors compared to reading/homework was 82.5 versus 48 minutes but the trend reversed from grade 1 with time spent on reading and homework increasing substantially with each schooling year (Figure 3). Compared to kindergarten, in year 9, time spent on reading was nearly 160 minutes but time outdoors reduced to 56.8 minutes.

Discussion

Our data for 606,476 children aged 4-14 years from the entire Shanghai region found 1in 3 children affected with myopia. At 8, 10 and 14 years of age, prevalence was significantly high at 16.8%, 36.5% and 72.3% for myopia and 0.7%, 2.7% and 15.2% for high myopia, respectively. Previously published data for myopia prevalence using cycloplegic refraction from Shanghai was reported to be approximately 30% and 52.2% at age 8 and 10 respectively and a later study reported a prevalence of

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15.2% in 8 year olds[17]. The current data using adjusted non-cycloplegic data and indicating high prevalence in young children is comparable to the previously reported data.

The results demonstrated a striking effect of schooling/education resulting in a more myopic refractive error. Using the discontinuity regression method, the study demonstrated a significant break point or a discontinuity in refractive error at September of each year, i.e. at the time children start a new school year. For each age category considered, children born pre-September were in a higher grade at school and had a more myopic refractive error compared to those born post 1 September. For those born pre-September, the refractive error was fairly similar and consistent irrespective of the birth month until the discontinuity point at September. The discontinuity or break point was observed commencing from age 6 onwards and reached approximately 0.5D at 13 years of age and 0.67D at 14 yrs. An association between myopia and years of schooling was previously reported [8-11]. Overall, entering the school a year early or being in one grade/class higher at school equated to approximately 0.67D more myopic refractive error by the time the child was 14 years of age. The threshold date of 1 September coinciding with the start of a new school year in a higher grade is likely associated with an increased academic workload such as greater amount of homework, greater class room workload or other assignments (for example, labs) and this load commonly increases with higher classes at schools. Indeed, data gathered from the questionnaire shows a steady increase in the time spent on homework from approximately 1 hour at 1st grade to nearly 2.5 hours at grade 8 to 9. Since the predominant form of high myopia in the cohort appears to be an extension of simple myopia, it therefore follows that if myopia is influenced by environmental factors including increased effort at educational tasks, then the same risk factors apply for high myopia[3].

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We reported on the prevalence of high myopia using both -5.00D cut-off [18] and -6.00D. Much of the previously reported data refers to -6.00D as the cut-off and using this criteria, the prevalence of high myopia in Shanghai among 14-year-olds children at 8.1% is higher than that reported from Singapore (4.7%, 14 year olds) [19], Hong Kong (3.8%, 12 year olds) [20], North America (2.0%, 10-14 years old) [18], Western Europe (2.5%, 10-14 years old) [18] and parts of China including Shandong (5.8%) [21], Ejina (5.2%) [22], Anyang (2.7%) [23] and Yunnan (1.3%) [24] but is comparable to the figures from Taiwan (7.8%) [25], Guangzhou (7%, 15 year olds) [4] and Beijing (9.4%) [1]. This data suggests that the burden of high myopia is set to increase in the future due to the current generation of highly myopic children aging and at risk of developing vision impairment and complications such as glaucoma, myopic maculopathy, retinal detachment and cataract. Although some of these complications may present in the young, they commonly manifest in adult life and therefore the need for monitoring and management significantly increases with age and therefore, there will be an increased need for highly skilled but scarce resources such as retinal surgeons, specialist ophthalmologists and rehabilitation services in the coming decades to manage complications and the resultant burden.

The study has several strengths and limitations. The large sample size across the various districts and ages presents us with an opportunity to determine disparities in prevalence within a region. Also, for the first time we described the use of regression discontinuity model to better understand the effect of education on myopia and refractive error. With respect to limitations, prevalence was determined with non-cycloplegic autorefraction that tends to overestimate the myopia prevalence especially in younger children. We took steps to minimize this bias by using a higher threshold to diagnose

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myopia (i.e. -1.0D rather than the usual -0.50D) and also applied an equation that considered uncorrected VA and age to reduce the risk [15]. However, Sankaridurg et al. 2017 reported that in spite of the corrective factor, there remained a risk of misclassification in about 20% especially with emmetropic and hyperopic eyes. Therefore, it is possible that our prevalence data may be subject to some errors and requires to be used with caution. Our study also used a questionnaire to gather data on risk factors. Such questionnaires are subject to various biases based on recall and qualitative nature of some of the questions (for example, sitting too close to television). More objective measurements using wearables that collect data on light exposure, physical activity etc. would provide more accurate estimates on behavior. Lastly, this was a cross-sectional study, and therefore, the causal effects of the observed associations could not be determined. Data from a follow-up visit conducted later is presently being analyzed and expected to provide further insights.

Conclusion

Our data demonstrated that the burden of myopia and high myopia in Shanghai is substantial and will grow in the future. We observed an association with education, that is, a myopic shift in refractive error is associated with each increasing school year and is reflective of increased near-work and decreased outdoor time observed with increasing age. There is an urgent need for public awareness and for reform of education systems to reduce or balance academic loads. In addition, health system should implement measures to monitor vision and refractive error progression in children to identify children at risk for management so as to reduce future increase in myopia. Finally, our study anticipated the need for increased services to cope with future rise in burden and could be help develop policies and systems to target the condition in an effective manner.

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Contributors: XX, HZ and JZ conceived the study. WL, SL and TN cleaned and analyzed the data. XH, PS and SX wrote the first draft of the manuscript. XX, HZ and JZ revised the draft. All authors contributed to data interpretation, critical revisions, and final approval of the manuscript. XX is the guarantor.

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Data availability statement: Data may be obtained from a third party and are not publicly available.

All data relevant to the study are included in the article.

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Figure legends:

Figure 1. Regression discontinuation analysis- Impact of education on spherical equivalent refractive error.

Figure 2. Difference in myopic refractive error between those born before or after September at a given age.

Figure 3. Figure. Average reading and outdoor time by grade.

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Table 1: Adjusted & Standardised Prevalence of Myopia and High Myopia by Age and Gender

		Myopia		High Myopia (≤ -5.00D)		High Myopia (≤ -6.00D)	
Age (yr.)	Num.	# Kids	% (95%CI)	# Kids	% (95%CI)	# Kids	% (95%CI)
4	16895	1246	7.1 (6.7 - 7.5)	122	0.7 (0.5 - 0.8)	65	0.4 (0.3 - 0.5)
5	50382	2968	5.7 (5.5 - 5.9)	212	0.4 (0.3 - 0.5)	134	0.3 (0.2 - 0.3)
6	59531	3821	6.1 (5.9 - 6.3)	267	0.4 (0.4 - 0.5)	160	0.3 (0.2 - 0.3)
7	73581	7135	9.4 (9.2 - 9.6)	396	0.5 (0.5 - 0.6)	237	0.3 (0.3 - 0.4)
8	74794	12445	16.8 (16.5 - 17.1)	514	0.7 (0.6 - 0.8)	286	0.4 (0.4 - 0.5)
9	72516	18912	26.0 (25.7 - 26.3)	942	1.3 (1.2 - 1.4)	442	0.6 (0.5 - 0.6)
10	62199	22822	36.5 (36.1 - 36.9)	1649	2.7 (2.5 - 2.8)	749	1.2 (1.1 - 1.3)
11	60492	29682	48.5 (48.1 - 48.9)	2679	4.3 (4.2 - 4.5)	1217	2.0 (1.9 - 2.1)
12	49386	28898	57.3 (56.9 - 57.7)	3626	7.1 (6.9 - 7.3)	1699	3.3 (3.2 - 3.5)
13	47253	32077	66.4 (66.0 - 66.9)	5478	11.0 (10.7 - 11.3)	2682	5.4 (5.2 - 5.6)
14	39447	29343	72.3 (71.9 - 72.8)	6419	15.2 (14.9 - 15.6)	3375	8.1 (7.8 - 8.4)
Total	606476	189349	32.9 (32.8 - 33.0)	22304	4.2 (4.1 - 4.2)	11046	2.1 (2.0 - 2.1)
Boys	322953	96555	31.5 (31.3 - 31.7)	10831	3.8 (3.8 - 3.9)	5382	1.9 (1.9 - 2.0)
Girls	283523	92794	34.6 (34.4 - 34.7)	11473	4.6 (4.5 - 4.6)	5664	2.3 (2.2 - 2.3)

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Table 2: Vision Impairment (VI) with Myopia and High myopia (based on visual acuity in the better eye)

Snellen VA (Five - grade notation)	VI based on Uncorrected Visual Acuity			VI based on Presenting Visual Acuity		
	No of children/% of entire sample	No of children with myopia/% of entire sample	No of children with high myopia/% of entire sample	No of children/% of entire sample	No of children with myopia/% of entire sample	No of children with high myopia/% of entire sample
6/9 (4.8) or better	486434 (80.2%)	82985 (13.6%)	3264 (0.54%)	544188 (89.7%)	137599 (22.7%)	15436 (2.6%)
6/9 to 6/12(4.7)	27629 (4.6%)	20121 (3.3%)	1057 (0.17%)	23212(3.8%)	16822 (2.8%)	1605 (0.26%)
<6/12(4.7) but 6/18(4.5)	41804 (6.9%)	37433 (6.2%)	3930 (0.65%)	23398 (3.9%)	20245(3.3%)	1967 (0.32%)
<6/18(4.5) but 6/60(4.0)	49655(8.2%)	48026 (7.9%)	13664 (2.3%)	15213 (2.5%)	14383 (2.4%)	3204 (0.53%)
<6/60(4.0) but 3/60(3.7)	488 (0.08%)	476 (0.07%)	296 (0.05%)	84 (0.01%)	75 (0.01 %%)	41 (0.01%)
<3/60(3.7)	466 (0.07%)	308 (0.05%)	93 (0.02%)	381 (0.06%)	225 (0.03%)	51 (0.01%)
Total	606476	189349	22304	606476	189349	22304

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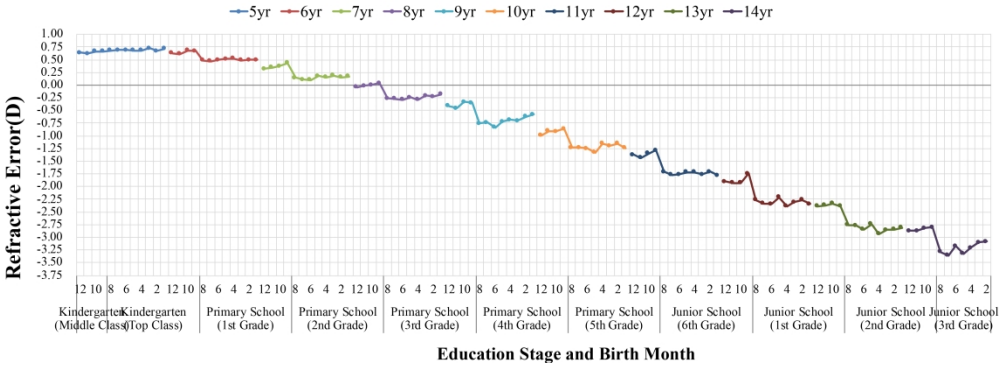
5yr
6yr
7yr
8yr
9yr
10yr
11yr
12yr
13yr
14yr
Refractive Error(D)
Kindergarten (Middle Class)
Kindergarten (Top Class)
Primary School (1st Grade)
Primary School (2nd Grade)
Primary School (3rd Grade)
Primary School (4th Grade)
Primary School (5th Grade)
Junior School (6th Grade)
Junior School (1st Grade)
Junior School (2nd Grade)
Junior School (3rd Grade)
Education Stage and Birth Month

Figure 1

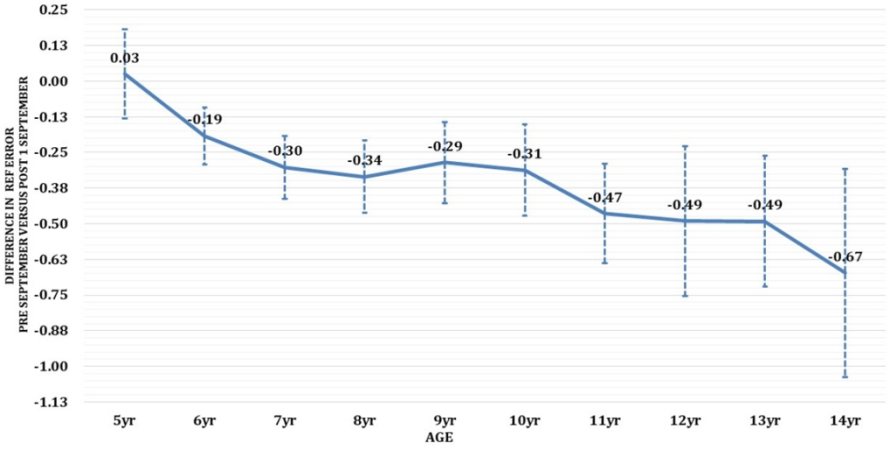

Figure 2

338x190mm (96 x 96 DPI)

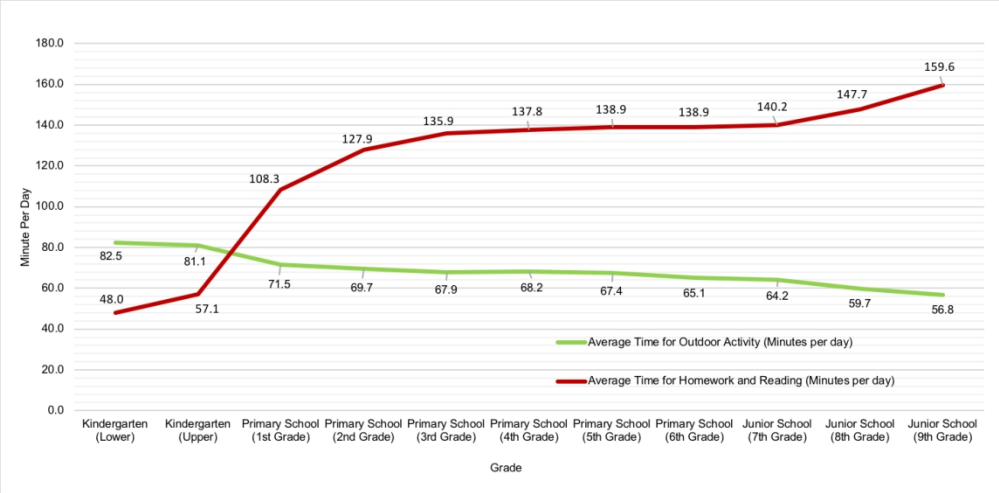

Figure 3

123x60mm (300 x 300 DPI)

Appendix Table 1. Distribution of Risk Factors in Children with and without Myopia and Multivariate Model of Myopia

Factors	No Myopia (n = 352265), % (n)	Myopia (n = 162879), % (n)	Odds ratio	95% CI	*P Value*
Age			0.04	0.04 - 0.05	<0.0001
4-6yrs	93.6 (103077)	6.4 (6999)	Reference		
7yrs	90.2 (56604)	9.8 (6168)	1.59	1.43 - 1.75	<0.0001
8yrs	83.0 (51480)	17.0 (10580)	2.99	2.74 - 3.27	<0.0001
9yrs	73.4 (44861)	26.6 (16284)	5.40	4.99 - 5.84	<0.0001
10yrs	62.3 (32437)	37.7 (19603)	9.43	8.72 - 10.21	<0.0001
11yrs	50.1 (25735)	49.9 (25620)	16.13	14.92 - 17.43	<0.0001
12yrs	40.9 (16978)	59.1 (24552)	24.11	22.11 - 26.29	<0.0001
13yrs	31.4 (12723)	68.6 (27819)	36.48	33.3 - 39.96	<0.0001
14yrs	24.9 (8370)	75.1 (25254)	50.75	46.27 - 55.67	<0.0001
Time for Playing and Entertainment (Hours per day)	1.85 ± 0.95 *	1.64 ± 0.89 *	0.92	0.91 - 0.93	<0.0001
Gender					
Male	69.8 (190002)	30.2 (82247)	Reference		
Female	66.8 (162263)	33.2 (80632)	1.16	1.14 - 1.19	<0.0001
Parental myopia					
Neither	71.0 (229036)	29.0 (93746)	Reference		
Either	65.0 (69677)	35.0 (37523)	1.60	1.53 - 1.68	<0.0001
Both	62.9 (53552)	37.1 (31610)	2.19	2.07 - 2.33	<0.0001
Month of the year born					
Before 1 September	68.2 (231833)	31.8 (108130)	Reference		
On or After 1 September	68.7 (120432)	31.3 (54749)	0.82	0.8 - 0.83	<0.0001
Rest after Continuous Use of Eye					
Never	66.5 (75717)	33.5 (38147)	Reference		

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Sometimes	67.2 (199536)	32.8 (97219)	0.96	0.94 - 0.98	<0.0001
Usually	73.7 (77012)	26.3 (27513)	0.80	0.78 - 0.82	<0.0001
Too Close to Book While Reading					
Never	71.8 (70303)	28.2 (27638)	Reference		
Sometimes	69.9 (206358)	30.1 (88806)	1.23	1.2 - 1.26	<0.0001
Usually	62.0 (75604)	38.0 (46435)	1.56	1.51 - 1.61	<0.0001
Too Close to Television While Watching					
Never	70.5 (129362)	29.5 (54217)	Reference		
Sometimes	68.4 (178596)	31.6 (82430)	1.21	1.18 - 1.23	<0.0001
Usually	62.8 (44307)	37.2 (26232)	1.38	1.33 - 1.42	<0.0001

CI = Confidence Interval

*mean ± SD

Myopia is defined as: Non Cyclo Sphere Equivalent <= (-1D)

Logistic Regression with Robust Estimation of Variance was used to count for correlation within cluster

AUC = 0.818

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Appendix Table 2. Distribution of Risk Factors in Children with and with no High Myopia and Multivariate Model of High Myopia

Factors	No High Myopia (n = 495558), % (n)	High Myopia (n = 19586), % (n)	Odds ratio	95% CI	*P Value*
Age			0.003	0.003 - 0.004	<0.0001
4-6yrs	99.5 (109545)	0.5 (531)	Reference		
7yrs	99.4 (62420)	0.6 (352)	1.14	0.96 - 1.36	0.1342
8yrs	99.3 (61626)	0.7 (434)	1.42	1.19 - 1.68	<0.0001
9yrs	98.7 (60323)	1.3 (822)	2.75	2.31 - 3.28	<0.0001
10yrs	97.2 (50577)	2.8 (1463)	6.05	5.05 - 7.25	<0.0001
11yrs	95.4 (48982)	4.6 (2373)	10.32	8.94 - 11.92	<0.0001
12yrs	92.4 (38380)	7.6 (3150)	17.95	15.68 - 20.56	<0.0001
13yrs	88.1 (35708)	11.9 (4834)	29.52	25.82 - 33.75	<0.0001
14yrs	83.3 (27997)	16.7 (5627)	44.43	38.91 - 50.74	<0.0001
Time for Playing and Entertainment (Hours per day)	1.79 ± 0.94 *	1.54 ± 0.88 *	0.90	0.88 - 0.93	<0.0001
Gender					
Male	96.5 (262805)	3.5 (9444)	Reference		
Female	95.8 (232753)	4.2 (10142)	1.16	1.12 - 1.2	<0.0001
Parental_myopia					
Neither	97.0 (313178)	3.0 (9604)	Reference		
Either	95.4 (102226)	4.6 (4974)	1.72	1.59 - 1.86	<0.0001
Both	94.1 (80154)	5.9 (5008)	2.62	2.4 - 2.87	<0.0001

Birth Time of the year					
Before September 1st	96.1 (326545)	3.9 (13418)	Reference		
After September 1st	96.5 (169013)	3.5 (6168)	0.77	0.75 - 0.8	<0.0001
Rest after Continuous Use of Eye					
Never	95.6 (108908)	4.4 (4956)	Reference		
Sometimes	96.1 (285151)	3.9 (11604)	0.97	0.93 - 1.01	0.1275
Usually	97.1 (101499)	2.9 (3026)	0.85	0.81 - 0.9	<0.0001
Too Close to Book While Reading					
Never	96.8 (94796)	3.2 (3145)	Reference		
Sometimes	96.5 (284773)	3.5 (10391)	1.22	1.16 - 1.27	<0.0001
Usually	95.0 (115989)	5.0 (6050)	1.58	1.5 - 1.67	<0.0001
Too Close to Television While Watching					
Never	96.3 (176834)	3.7 (6745)	Reference		
Sometimes	96.3 (251251)	3.7 (9775)	1.07	1.03 - 1.11	0.0002
Usually	95.7 (67473)	4.3 (3066)	1.06	1 - 1.12	0.0460

CI = Confidence Interval

*mean ± SD

High Myopia is defined as: Non Cyclo Sphere Equivalent <= (-5D)

Logistic Regression with Robust Estimation of Variance was used to count for correlation within cluster

AUC = 0.833

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation
√Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found
Introduction		
√Background/rationale	2	Explain the scientific background and rationale for the investigation being reported
√Objectives	3	State specific objectives, including any prespecified hypotheses
Methods		
√Study design	4	Present key elements of study design early in the paper
√Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection
√Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants
√Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable
√Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group
√Bias	9	Describe any efforts to address potential sources of bias
√Study size	10	Explain how the study size was arrived at
√Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why
√Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding
		(*b*) Describe any methods used to examine subgroups and interactions
		(*c*) Explain how missing data were addressed
		(*d*) If applicable, describe analytical methods taking account of sampling strategy
		(*e*) Describe any sensitivity analyses
Results		
√Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed
		(b) Give reasons for non-participation at each stage
		(c) Consider use of a flow diagram
√Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders
		(b) Indicate number of participants with missing data for each variable of interest
√Outcome data	15*	Report numbers of outcome events or summary measures
√Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included
		(*b*) Report category boundaries when continuous variables were categorized
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
√Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses

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Discussion		
√Key results	18	Summarise key results with reference to study objectives
√Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias
√Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence
√Generalisability	21	Discuss the generalisability (external validity) of the study results
Other information		
√Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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The prevalence of myopia and high myopia, and the association with education: Shanghai Child and Adolescent Large-scale Eye Study (SCALE), a cross-sectional study

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Primary Subject Heading:	Ophthalmology
Secondary Subject Heading:	Epidemiology, Public health
Keywords:	OPHTHALMOLOGY, PUBLIC HEALTH, EPIDEMIOLOGY

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The prevalence of myopia and high myopia, and the association with education: Shanghai Child and Adolescent Large-scale Eye Study (SCALE), a cross-sectional study

Running title: high myopia and education

Xiangui He[1,2] PhD, Padmaja Sankaridurg[3,4] PhD, Shuyu Xiong[2] PhD, Wayne Li[3,4] MD, Thomas Naduvilath[3,4] PhD, Senlin Lin[1] MSc, Rebecca Weng[3,4] GD, Minzhi Lv[1] MPH, Yingyan Ma[2] PhD, Lina Lu[1] MPH, Jingjing Wang[1] MPH, Rong Zhao[1] JM, Serge Resnikoff[3,4] PhD, Jianfeng Zhu[1]* MD, Haidong Zou [1,2]* MD, Xun Xu[1,2]* MD

Xiangui He and Padmaja Sankaridurg are equal first authors.

1. Department of Preventative Ophthalmology, Shanghai Eye Disease Prevention and Treatment Center, Shanghai Eye Hospital, Shanghai, China
2. Department of Ophthalmology, Shanghai Key Laboratory of Ocular Fundus Disease, Shanghai General Hospital, Shanghai Engineering Center for Visual Science and Photomedicine, Shanghai Jiao Tong University, Shanghai, China； National Clinical Research Center for Eye Diseases, Shanghai, China.
3. Brien Holden Vision Institute, Sydney, New South Wales, Australia
4. School of Optometry and Vision Science, University of New South Wales, Sydney, New South Wales, Australia

Corresponding:

Xun Xu, Email: drxuxun@sjtu.edu.cn

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Haidong Zou，Email: zouhaidong@sjtu.edu.cn

Jianfeng Zhu，Email: jfzhu1974@hotmail.com

Address: No. 380 Kangding Road, Shanghai, 200040, China； Telephone: +86 021-62539696

Word count: text only: 2998, tables: 2, figures: 3

Key word: children, high myopia, education

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Abstract

Objectives: To report on: a) overall myopia and high myopia prevalence, and b) the impact of education on the spherical equivalent refractive error in children across Shanghai.

Design: Cross-sectional study.

Setting: Across all 17 districts of Shanghai.

Participants: 910,245 children aged 4 to14 years from a school-based survey conducted between 2012 and 2013.

Main outcome measures: Data of children with non-cycloplegic auto refraction, visual acuity assessment and questionnaire were analyzed (67%, n=606,476). Prevalence of myopia (≤-1.0D) and high myopia (≤-5.0D) was determined. We used a regression discontinuity design to determine the impact of school entry cut-off date (1 September) by comparing refractive errors at each age, for children born pre-September to post 1-September, and performed a multivariate analysis to explore risk factors associated with myopia. Data analysis was performed in 2017-2018.

Results: Prevalence of myopia and high myopia was 32.9% (95% CI:32.8-33.1) and 4.2% (95% CI:4.1-4.2) respectively. From 6 years of age onwards, children born pre-September were more myopic compared to those born post 1 September (ahead in school by one year, discontinuity at 6 yrs:-0.19D (95% CI: -0.09 to-0.30D);14 yrs:-0.67D (95% CI: -0.21 to-1.14D)).

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Conclusions: Our findings suggest that myopia is associated with education, that is primarily focused on near based activities. Efforts to reduce the burden should be directed to public awareness, reform of education and health systems.

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Strengths and limitations of this study

1. The large sample size across the various districts and ages presents us with an opportunity to determine disparities in prevalence within a region.

2. For the first time, we described the use of regression discontinuity model to better understand the effect of education on myopia and refractive error.

3. Prevalence was determined with non-cycloplegic autorefraction that tends to overestimate the myopia prevalence especially in younger children.

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Introduction

The intractable and escalating rise in the prevalence of myopia is fueling a public health crisis worldwide. In many East and South East Asian countries, including certain parts of China, the prevalence is nearly 80% among children aged 17-18 years. Although the prevalence differs geographically, myopia is prevalent and rising in many other parts of the world, including North America, Australia, Europe and Middle East.[1-4] For 2015 alone, the global burden related to myopia was estimated at US244 billion.[5] Most alarmingly, the recent decades have seen a trend with myopia presenting at younger ages than before and consequently, there is a higher overall risk of the individual eye reaching high myopia.[1 4] In younger individuals, high myopia increases the risk of retinal breaks and retinal detachment, whereas in older individuals, there is an increased risk for a myriad of complications such as glaucoma, cataract, and myopic maculopathy. Indeed, myopic maculopathy is already one of the leading causes of low vision and blindness among working adults in China and South East Asian region.[6 7]

It is well known that environmental factors such as time outdoors, socio-economic status, and urban location are significant risk factors for myopia and high myopia. Although a number of studies reported an association between education and myopia,[8-11] there is lack of direct evidence that schooling results in a more myopic refractive error in younger school-aged children, as well as the impact of early education, including education in kindergarten and primary school, which would be more important for myopia prevention in children. There is a need to better understand the influence of education as they aid in developing interventions to better address the growing burden of myopia.

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The Shanghai Child and Adolescent Large Eye Study is a large-scale, prospective, school-based survey undertaken across all 17 districts of Shanghai that provides the prevalence estimates for 606,476 children aged 4 to 14 years. In this article we present the overall prevalence of myopia, report the prevalence across the districts and determine the effect of schooling on refractive error.

Materials and methods

Study Overview

Detailed methods of the study were previously reported [12]. Briefly at the first visit undertaken in 2012 to 2013, it was aimed to screen all children aged 4 to14 years, from kindergarten to junior high, from all the 17 districts and counties of Shanghai, China. All schools and kindergartens, including the school for blind and vision impaired children were involved in the study. The Institutional Ethics Committee of Shanghai General Hospital, Shanghai Jiaotong University approved the protocol (ID: 2015KY149) and the study followed the tenets of the Declaration of Helsinki for experimentation on humans. Written consent was obtained from at least one parent/carer. Parents were informed of the study prior to any examination. Details of the process were explained in the methodology article published previously, where related supporting information has also been provided[12].

Data Collection

For each participant, both unaided and presenting (i.e., with a corrective device if worn) visual acuity (VA) was measured and parents/carers were required to fill in a simple questionnaire in consultation with the child. The questionnaire was designed to elicit known risk factors and behavioral patterns of

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the child and details of the questionnaire were presented previously.[12] Distance VA was measured using a standard logarithmic visual acuity E chart (National Standard of People's Republic of China, GB 11533-1989) mounted on an illuminated cabinet with a luminance of 80-320 cd/m^2. Refraction was conducted using either the Topcon KR-8900 (Tokyo, Japan), Nidek AR-330A (Nagoya, Japan) or HUVITZ HRK-7000A (Gemjeong-dong, South Korea) auto refractors. Measurements taken with these auto refractors were found comparable [13]. The procedure adopted for quality control was previously presented [12].

Definitions

VA in the better eye was used and the prevalence of vision impairment (VI) was calculated based both uncorrected and presenting VA. Definitions for VI were in accordance with WHO criteria: no VI defined as 6/12 or better, mild VI as worse than 6/12 to 6/18 inclusive, moderate VI as worse than 6/18 to 6/60 inclusive, severe as worse than 6/60 to 3/60 inclusive, and blindness defined as worse than 3/60 [14].

Prevalence of myopia and high myopia was determined using spherical equivalent refractive error (SE) based on non-cycloplegic autorefraction. Myopia and high myopia were defined as SE of ≤ -1.0D and ≤ -5.0D in either eye respectively. To enable comparisons with previously published data, we also determined the prevalence of high myopia wherein SE was ≤ -6.00D. Since non-cycloplegic refraction overestimates myopia we applied an equation to correct for the overestimation, with the equation based on data gathered from a subset of 6017 children from Shanghai of similar ages whose

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refractive errors were measured using both non-cycloplegia and cycloplegia. The model used non-cycloplegic refractive error, age and uncorrected VA to arrive at the equation [15]:

Equation 1

$$y = 0.831 + (0.954 \times \text{non cycloplegic SE}) + (-0.065 \times \text{age}) + (0.539 \times \text{UCVA})$$

$$R^2 = 0.91, \text{(Eq, 1, where y = cycloplegic SE)}$$

This adjustment provided an improved and conservative estimate of the myopia prevalence rather than that based on non-cycloplegic refraction alone.

Statistical Analysis

Prevalence of myopia and high myopia was determined by age, gender and district and were adjusted using equation 1 and further standardized to the age-gender distribution of all eligible children (1.19 million) in Shanghai. The 95% confidence limits were based on Wilson Score method [16]. The data for the 145 blind/vision impaired children was included in the vision impairment assessment but not for analysis related to prevalence of myopia and high myopia.

Association of demographic and behavioral factors with myopia and high myopia was explored using univariate and multivariate analysis with factors at $p<0.05$ included in the multivariate analysis. Model was developed using logistic regression and standard errors adjusted using robust estimation of variance for the clustering effects within each school. Steps included backward elimination followed by forward entry until only significant factors remained and strength of association was described using odds ratio (OR) and 95% CI. Area under ROC curve was the indicator for model discrimination. Statistical significance was set at 0.01.

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The interrelationship between age, education and refractive error was evaluated using a regression discontinuity (RD) model. RD model is used to estimate the impact of a policy or program in situations where exposure to a risk factor is based on whether they exceed or fall behind a designated cut-off point. In the present analysis, we considered education as a risk factor. Children born in a given year (same age) were assigned to either pre or post-September groups based on the school entry cut-off criteria of 1 September; those born pre-September are admitted to a higher class/grade compared to those born on or post 1 September. Thus, the aim was to determine if for a given age, children born pre- September had a more myopic refractive error compared to post-September as they were in a higher class at school (greater academic load). Therefore, 1st September was the cut-off point and refractive error was the outcome. The difference in refractive error pre and post September 1 is a measure of the effect of education on refractive error. For each age group, RD was used to model the effect of discontinuity on refractive error (difference of mean RE and 95% CI) at the cut-off point. The RD model used non parametric local polynomial regression where weights for each data reduce as they move further from the cut-off point and the size of each bin to estimate the discontinuity effect is determined using mean square error.[17]

Data cleaning and analysis were performed using SAS 9.3 (SAS Institute, Cary, NC, USA) and R3.2.0 (Vienna, Austria) in 2017-2018.

Patient and public involvement

Participants and the public were not involved in the design or planning of the study. The study had no patient advisers. Participants were not involved in recruiting other participants or conduct of the study. The study results are not planned to be disseminated to the participants.

Results

Study Population

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Of the 1,196,763 eligible children in Shanghai during the study period, a total of 910,245 children, with a mean age of 9.0 ± 2.8 yrs, and a male-female ratio of 53.3:46.7 were enrolled. A total of 2002 schools (average of 452 children per school) participated and the distribution of the population across the ages was previously presented [12]. Of the data for the 910,245 children, only data from 606,476 children (66.6%) was complete with both visual acuity and non-cycloplegic refraction data. The mean age of these children was 9.1 ± 2.8 yrs and gender distribution was 53.3:46.7 for males versus females and was comparable to the larger sample of 910,245 children.

Prevalence of Myopia and High Myopia

The overall adjusted and standardized prevalence of myopia was 32.9% (95% CI: 32.8-33.1).

The adjusted mean SE was -0.57 ± 1.99D (range: -22.4 to +15.5D). Table 1 presents the age and gender wise distribution of adjusted myopia prevalence and shows that prevalence increased with age with nearly 50% of 11-year-olds having myopia. Slightly greater prevalence was observed in females ($p < 0.001$).

The adjusted prevalence of high myopia (≤-5.00D) was 4.2% (95% CI: 4.1-4.2). Prevalence of high myopia was low until age 8 (<1%) and increased in prevalence thereafter to approximately 10% or more from age 13 and reached 15.2% in 14-year-olds. When using a higher cut-off criteria of ≤-6.00D, the adjusted prevalence fell to 2.1% (95% CI: 2.0-2.1). With the higher cut-off threshold, high myopia was observed in less than 1% of the cohort until age 9 and thereafter, increased steadily reaching a prevalence of 8.1% in 14-year-olds.

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Considering uncorrected VA, of the 606,476 children, 92,413 (15.3% of entire sample) had VA ≤ 6/12 which was mostly due to myopia (86,243 eyes, 14.2% of entire sample). Similarly, when presenting VA was considered, 39,076/606,476 (6.4% of entire sample) had VA ≤ 6/12 of which 34,298 or 5.7% of entire sample were myopic (Table 2).

Risk Factors Associated with Myopia and High Myopia

Age was the most significant predictive factor for both myopia and high myopia. Compared to a child aged 4-6 years, at 9 years, the odds ratio of having myopia increased by 5 times and to 50 times at 14 years of age (OR=50.9, 95% CI: 46.6-55.7; p<0.0001) (Appendix Table 1). Similarly, for high myopia, compared to a child aged 4-6 years, at 9 years of age, the odds ratio for high myopia was 3 times greater and was 44 times greater at 14 years of age (OR=44.1, 38.6-50.3; p<0.0001) (Appendix Table 2).

Of the other risk factors, females had a 20% greater risk of being myopic and highly myopic (for both myopia and high myopia: OR=1.2, 1.1-1.2, p<0.0001). Moreover, having either one or both parents myopic increased the odds of myopia in children by 1.6 and 2.2 times compared to children with no myopic parent. A similar trend but slightly higher odds was observed for high myopia, where children with one or both myopic parents having a higher risk by 1.7 and 2.6 times.

Behavioral factors such as holding a book too close while reading increased the odds for myopia by 20 to 50% and watching television at close distances increased the odds by 10 to 40%. Interestingly, having a rest after continuous was protective by 3 to 20% and time playing and in entertainment was also mildly protective (10%). The increase or decrease in odds were similar for both myopia and

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high myopia suggesting that the behavioral factors experienced and found influencing prevalence were the same.

Additionally, children born post 1September in a calendar year had a 18 to 23% lower risk of being myopic compared to those born pre-September.

Estimating the effect of School start date on SE refractive error

Figure 1 shows the effect of school start date in September on SE refractive error. Considering the case of 6-year-olds, it is seen that those that born pre- September (corresponding to the vertical grid line) were in 1st grade of primary school and had a more myopic SE whereas those born post-September were in Upper Kindergarten and had a less myopic refractive error. Overall, as children progressed through the school years (or grades) refractive error became more myopic and importantly, the myopic shift in refractive error at the September cut-off point became more pronounced with older children having a significant discontinuity or a much greater difference in refractive error at the 1 September cut-off date.

Figure 2 presents the observed data for each age group and the polynomial line based on the local polynomial regression used in the regression discontinuity model. The graphs illustrate a significant discontinuity at 1September where the intercept of the polynomial shows a lower refractive error post 1 September. Figure 3 summarizes the difference in refractive error for those born pre-September compared to post 1 September. Those born before September 1 had a more myopic refractive error by approximately 0.2D at 6 years of age and this difference increased steadily with age and reached approximately 0.5D at 13 years of age and nearly 0.7 D at 14 years of age.

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Using data gathered from the questionnaire, it was seen that during the kindergarten years, time spent outdoors compared to reading/homework was 82.5 versus 48 minutes but the trend reversed from grade 1 with time spent on reading and homework increasing substantially with each schooling year (Figure 4). Compared to kindergarten, in year 9, time spent on reading was nearly 160 minutes but time outdoors reduced to 56.8 minutes.

Discussion

Our data for 606,476 children aged 4-14 years from the entire Shanghai region found 1in 3 children affected with myopia. At 8, 10 and 14 years of age, prevalence was significantly high at 16.8%, 36.5% and 72.3% for myopia and 0.7%, 2.7% and 15.2% for high myopia, respectively. Previously published data for myopia prevalence (-1.0D or worse) and using cycloplegic refraction from Shanghai was reported to be approximately 21.9% and 41.8% at ages 8 and 10 respectively [18]. The current data using adjusted non-cycloplegic data and indicating high prevalence in young children is a more conservative estimate compared to the previously reported data.

The results demonstrated a striking effect of schooling/education resulting in a more myopic refractive error. Using the discontinuity regression method, the study demonstrated a significant break point or a discontinuity in refractive error at September of each year, i.e. at the time children start a new school year. For each age category considered, children born pre-September were in a higher grade at school and had a more myopic refractive error compared to those born post 1 September. For those born pre-September, the refractive error was fairly similar and consistent irrespective of the birth month until the discontinuity point at September. The discontinuity or break

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point was observed commencing from age 6 onwards and reached approximately 0.5D at 13 years of age and 0.67D at 14 yrs. An association between myopia and years of schooling was previously reported [8-11]. Overall, entering the school a year early or being in one grade/class higher at school equated to approximately 0.67D more myopic refractive error by the time the child was 14 years of age. The threshold date of 1 September coinciding with the start of a new school year in a higher grade is likely associated with an increased academic workload such as greater amount of homework, greater class room workload or other assignments (for example, labs) and this load commonly increases with higher classes at schools. Indeed, data gathered from the questionnaire shows a steady increase in the time spent on homework from approximately 1 hour at 1st grade to nearly 2.5 hours at grade 8 to 9. Since the predominant form of high myopia in the cohort appears to be an extension of simple myopia, it therefore follows that if myopia is influenced by environmental factors including increased effort at educational tasks, then the same risk factors apply for high myopia[3].

We reported on the prevalence of high myopia using both -5.00D cut-off [19] and -6.00D. Much of the previously reported data refers to -6.00D as the cut-off and using this criteria, the prevalence of high myopia in Shanghai among 14-year-olds children at 8.1% is higher than that reported from Singapore (4.7%, 14 year olds) [20], Hong Kong (3.8%, 12 year olds) [21], North America (2.0%, 10-14 years old) [19], Western Europe (2.5%, 10-14 years old) [19] and parts of China including Shandong (5.8%) [22], Ejina (5.2%) [23], Anyang (2.7%) [24] and Yunnan (1.3%) [25] but is comparable to the figures from Taiwan (7.8%) [26], Zhejiang (10.4%) [27], Tianjin (6.1%) [28], Guangzhou (7%, 15 year olds) [4] and Beijing (9.4%) [1] (Figure 5). This data suggests that the burden of high myopia is set to increase in the future due to the current generation of highly myopic children aging and at risk of developing vision

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impairment and complications such as glaucoma, myopic maculopathy, retinal detachment and cataract. Although some of these complications may present in the young, they commonly manifest in adult life and therefore the need for monitoring and management significantly increases with age and therefore, there will be an increased need for highly skilled but scarce resources such as retinal surgeons, specialist ophthalmologists and rehabilitation services in the coming decades to manage complications and the resultant burden.

The study has several strengths and limitations. The large sample size across the various districts and ages presents us with an opportunity to determine disparities in prevalence within a region. Also, for the first time we described the use of regression discontinuity model to better understand the effect of education on myopia and refractive error. With respect to limitations, prevalence was determined with non-cycloplegic autorefraction that tends to overestimate the myopia prevalence especially in younger children. We took steps to minimize this bias by applying an equation that considered uncorrected VA and age to reduce the risk [15]. However, Sankaridurg et al. 2017 reported that using -0.75D as the criteria to categorise myopia, in spite of the corrective factor, there remained a risk of misclassification in about 20% especially with emmetropic and hyperopic eyes. Therefore, we used a higher threshold to diagnose myopia (i.e. -1.0D rather than the usual -0.50D) to improve the sensitivity. However, it is possible that our prevalence data may still be subject to some errors and requires to be used with caution. Our study also used a questionnaire to gather data on risk factors. Such questionnaires are subject to various biases based on recall and the qualitative nature of some of the questions (for example, sitting too close to television), are differential and could possibly overestimate or underestimate related parameters. More objective measurements using wearables

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that collect data on light exposure, physical activity etc. would provide more accurate estimates on behavior. Additionally, the regression discontinuity analysis may have been affected by factors stemming from asymmetry of data gathered pre-September versus post September. For example, there is data from more months pre-September versus post- September. The analysis used a local-polynomial estimator, wherein data closer to the cut-off point of 1 September are weighted more than points further away and therefore we believe that asymmetry would not affect the estimation substantially. However, there may be other factors such as variation in birth rates that may influence- we had not considered the impact of such factors. Lastly, this was a cross-sectional study, and therefore, the causal effects of the observed associations could not be determined. Data from a follow-up visit conducted later is presently being analyzed and expected to provide further insights.

Conclusion

Our data demonstrated that the burden of myopia and high myopia in Shanghai is substantial and will grow in the future. We observed an association with education, that is, a myopic shift in refractive error is associated with each increasing school year and is reflective of increased near-work and decreased outdoor time observed with increasing age. There is an urgent need for public awareness and for reform of education systems to reduce or balance academic loads. In addition, health system should implement measures to monitor vision and refractive error progression in children to identify children at risk for management so as to reduce future increase in myopia. Finally, our study anticipated the need for increased services to cope with future rise in burden and could be help develop policies and systems to target the condition in an effective manner.

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Patient consent for publication: Not required.

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Ethics approval: The Institutional Ethics Committee of Shanghai General Hospital, Shanghai Jiaotong University approved the protocol.

Data availability statement: Data may be obtained from a third party and are not publicly available. All data relevant to the study are included in the article.

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Figure legends:

Figure 1. Regression discontinuation analysis- Impact of education on spherical equivalent refractive error.

Figure 2. Estimated polynomial line using regression discontinuity model illustrating discontinuity in refractive error at 1 September for each age. Dots denote observed data

Figure 3. Estimated difference in refractive error for those born pre versus post 1 September for each ageage as determined using regression discontinuity model. Error bars represent 95% CI.

Figure 4. Average reading and outdoor time by grade.

Figure 5: Myopia prevalence (SE ≤ -6.00D) in areas of South East Asia.

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Table 1: Adjusted & Standardised Prevalence of Myopia and High Myopia by Age and Gender

		Myopia		High Myopia (≤ -5.00D)		High Myopia (≤ -6.00D)	
Age (yr.)	Num.	# Kids	% (95%CI)	# Kids	% (95%CI)	# Kids	% (95%CI)
4	16895	1246	7.1 (6.7 - 7.5)	122	0.7 (0.5 - 0.8)	65	0.4 (0.3 - 0.5)
5	50382	2968	5.7 (5.5 - 5.9)	212	0.4 (0.3 - 0.5)	134	0.3 (0.2 - 0.3)
6	59531	3821	6.1 (5.9 - 6.3)	267	0.4 (0.4 - 0.5)	160	0.3 (0.2 - 0.3)
7	73581	7135	9.4 (9.2 - 9.6)	396	0.5 (0.5 - 0.6)	237	0.3 (0.3 - 0.4)
8	74794	12445	16.8 (16.5 - 17.1)	514	0.7 (0.6 - 0.8)	286	0.4 (0.4 - 0.5)
9	72516	18912	26.0 (25.7 - 26.3)	942	1.3 (1.2 - 1.4)	442	0.6 (0.5 - 0.6)
10	62199	22822	36.5 (36.1 - 36.9)	1649	2.7 (2.5 - 2.8)	749	1.2 (1.1 - 1.3)
11	60492	29682	48.5 (48.1 - 48.9)	2679	4.3 (4.2 - 4.5)	1217	2.0 (1.9 - 2.1)
12	49386	28898	57.3 (56.9 - 57.7)	3626	7.1 (6.9 - 7.3)	1699	3.3 (3.2 - 3.5)
13	47253	32077	66.4 (66.0 - 66.9)	5478	11.0 (10.7 - 11.3)	2682	5.4 (5.2 - 5.6)
14	39447	29343	72.3 (71.9 - 72.8)	6419	15.2 (14.9 - 15.6)	3375	8.1 (7.8 - 8.4)
Total	606476	189349	32.9 (32.8 - 33.0)	22304	4.2 (4.1 - 4.2)	11046	2.1 (2.0 - 2.1)
Boys	322953	96555	31.5 (31.3 - 31.7)	10831	3.8 (3.8 - 3.9)	5382	1.9 (1.9 - 2.0)
Girls	283523	92794	34.6 (34.4 - 34.7)	11473	4.6 (4.5 - 4.6)	5664	2.3 (2.2 - 2.3)

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Table 2: Vision Impairment (VI) with Myopia and High myopia (based on visual acuity in the better eye)

Snellen VA (Five - grade notation)	VI based on Uncorrected Visual Acuity			VI based on Presenting Visual Acuity		
	No of children/% of entire sample	No of children with myopia/% of entire sample	No of children with high myopia/% of entire sample	No of children/% of entire sample	No of children with myopia/% of entire sample	No of children with high myopia/% of entire sample
6/9 (4.8) or better	486434 (80.2%)	82985 (13.6%)	3264 (0.54%)	544188 (89.7%)	137599 (22.7%)	15436 (2.6%)
6/9 to 6/12(4.7)	27629 (4.6%)	20121 (3.3%)	1057 (0.17%)	23212(3.8%)	16822 (2.8%)	1605 (0.26%)
<6/12(4.7) but 6/18(4.5)	41804 (6.9%)	37433 (6.2%)	3930 (0.65%)	23398 (3.9%)	20245(3.3%)	1967 (0.32%)
<6/18(4.5) but 6/60(4.0)	49655(8.2%)	48026 (7.9%)	13664 (2.3%)	15213 (2.5%)	14383 (2.4%)	3204 (0.53%)
<6/60(4.0) but 3/60(3.7)	488 (0.08%)	476 (0.07%)	296 (0.05%)	84 (0.01%)	75 (0.01 %%)	41 (0.01%)
<3/60(3.7)	466 (0.07%)	308 (0.05%)	93 (0.02%)	381 (0.06%)	225 (0.03%)	51 (0.01%)
Total	606476	189349	22304	606476	189349	22304

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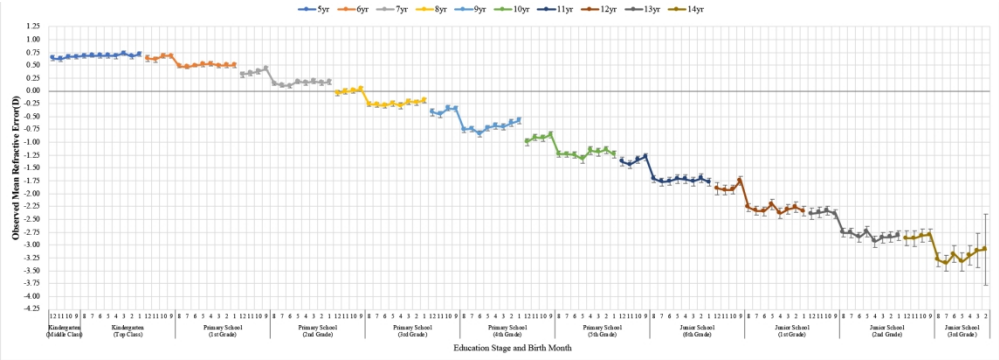

Figure 1

172x61mm (300 x 300 DPI)

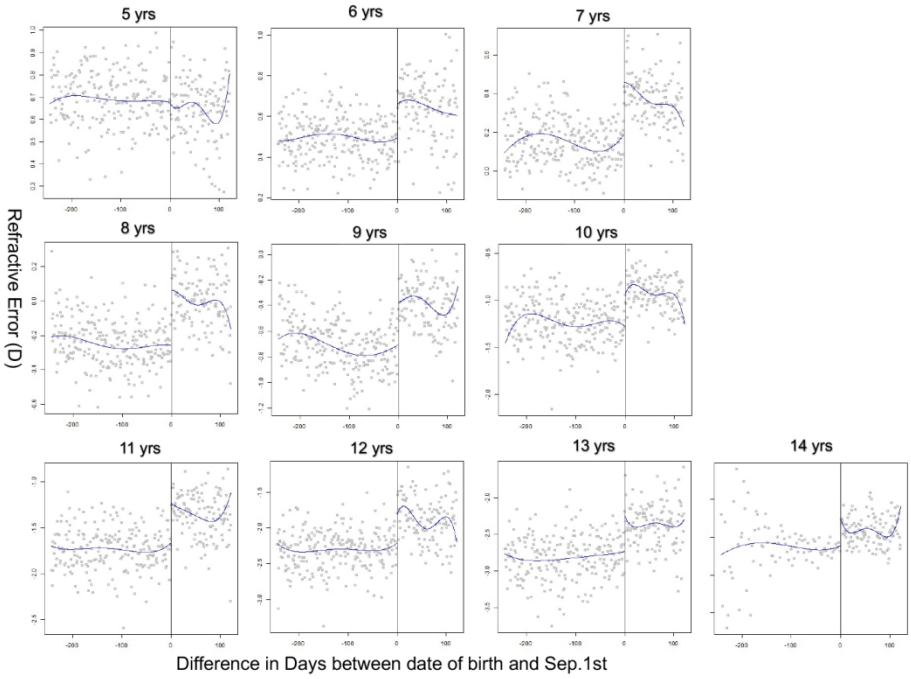

Figure 2

135x96mm (300 x 300 DPI)

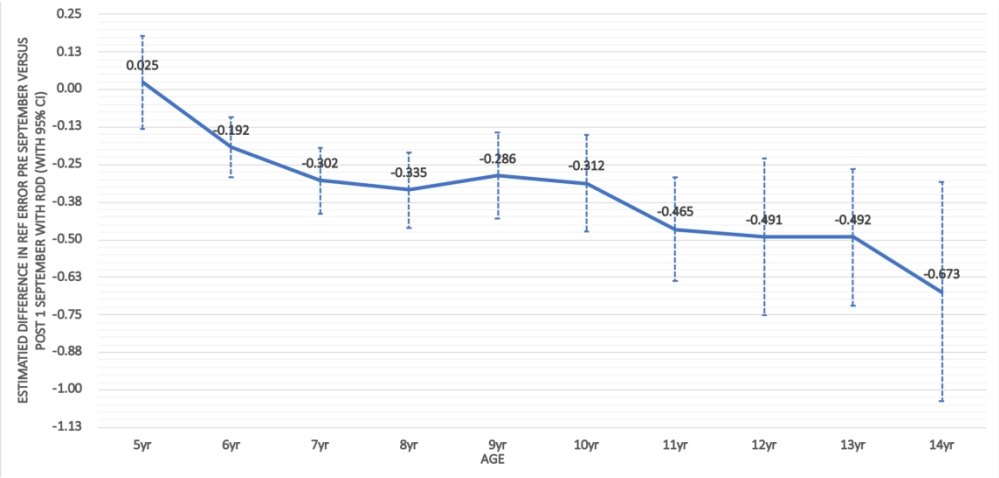

Figure 3

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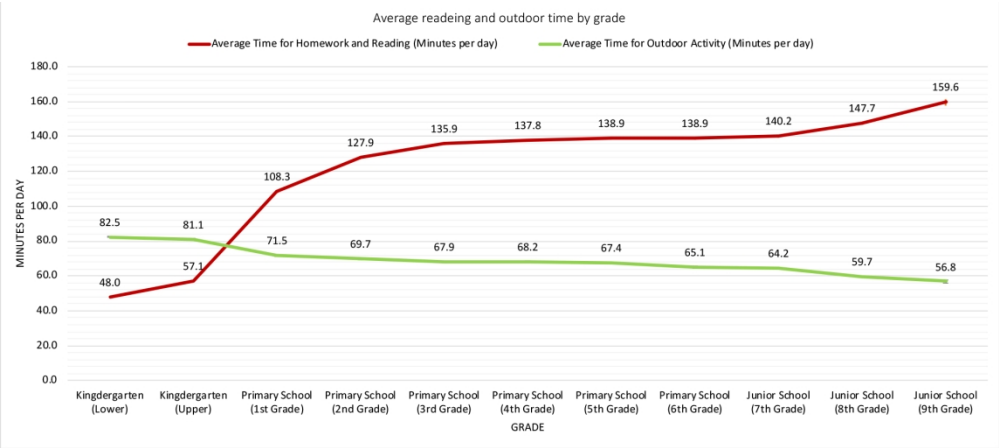

Figure 4

172x76mm (300 x 300 DPI)

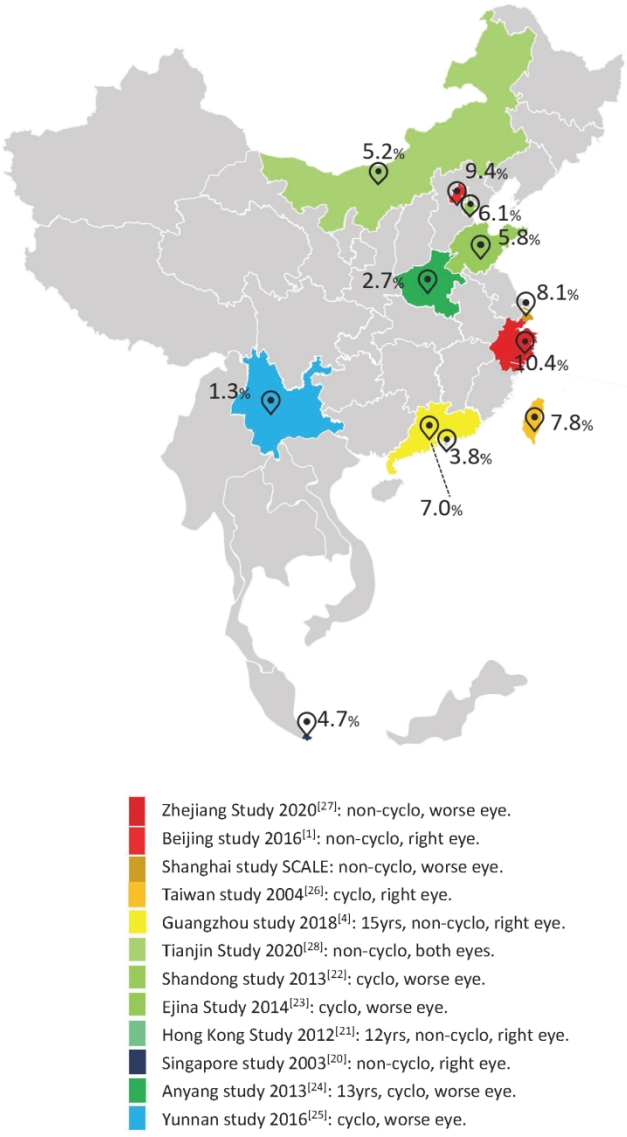

Figure 5

158x235mm (252 x 252 DPI)

Appendix Table 1. Distribution of Risk Factors in Children with and without Myopia and Multivariate Model of Myopia

Factors	No Myopia (n = 352265), % (n)	Myopia (n = 162879), % (n)	Odds ratio	95% CI	*P Value*
Age			0.04	0.04 - 0.05	<0.0001
4-6yrs	93.6 (103077)	6.4 (6999)	Reference		
7yrs	90.2 (56604)	9.8 (6168)	1.59	1.43 - 1.75	<0.0001
8yrs	83.0 (51480)	17.0 (10580)	2.99	2.74 - 3.27	<0.0001
9yrs	73.4 (44861)	26.6 (16284)	5.40	4.99 - 5.84	<0.0001
10yrs	62.3 (32437)	37.7 (19603)	9.43	8.72 - 10.21	<0.0001
11yrs	50.1 (25735)	49.9 (25620)	16.13	14.92 - 17.43	<0.0001
12yrs	40.9 (16978)	59.1 (24552)	24.11	22.11 - 26.29	<0.0001
13yrs	31.4 (12723)	68.6 (27819)	36.48	33.3 - 39.96	<0.0001
14yrs	24.9 (8370)	75.1 (25254)	50.75	46.27 - 55.67	<0.0001
Time for Playing and Entertainment (Hours per day)	1.85 ± 0.95 *	1.64 ± 0.89 *	0.92	0.91 - 0.93	<0.0001
Gender					
Male	69.8 (190002)	30.2 (82247)	Reference		
Female	66.8 (162263)	33.2 (80632)	1.16	1.14 - 1.19	<0.0001
Parental myopia					
Neither	71.0 (229036)	29.0 (93746)	Reference		
Either	65.0 (69677)	35.0 (37523)	1.60	1.53 - 1.68	<0.0001
Both	62.9 (53552)	37.1 (31610)	2.19	2.07 - 2.33	<0.0001
Month of the year born					
Before 1 September	68.2 (231833)	31.8 (108130)	Reference		
On or After 1 September	68.7 (120432)	31.3 (54749)	0.82	0.8 - 0.83	<0.0001
Rest after Continuous Use of Eye					
Never	66.5 (75717)	33.5 (38147)	Reference		

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Sometimes	67.2 (199536)	32.8 (97219)	0.96	0.94 - 0.98	<0.0001
Usually	73.7 (77012)	26.3 (27513)	0.80	0.78 - 0.82	<0.0001
Too Close to Book While Reading					
Never	71.8 (70303)	28.2 (27638)	Reference		
Sometimes	69.9 (206358)	30.1 (88806)	1.23	1.2 - 1.26	<0.0001
Usually	62.0 (75604)	38.0 (46435)	1.56	1.51 - 1.61	<0.0001
Too Close to Television While Watching					
Never	70.5 (129362)	29.5 (54217)	Reference		
Sometimes	68.4 (178596)	31.6 (82430)	1.21	1.18 - 1.23	<0.0001
Usually	62.8 (44307)	37.2 (26232)	1.38	1.33 - 1.42	<0.0001

CI = Confidence Interval

*mean ± SD

Myopia is defined as: Non Cyclo Sphere Equivalent <= (-1D)

Logistic Regression with Robust Estimation of Variance was used to count for correlation within cluster

AUC = 0.818

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Appendix Table 2. Distribution of Risk Factors in Children with and with no High Myopia and Multivariate Model of High Myopia

Factors	No High Myopia (n = 495558), % (n)	High Myopia (n = 19586), % (n)	Odds ratio	95% CI	*P Value*
Age			0.003	0.003 - 0.004	<0.0001
4-6yrs	99.5 (109545)	0.5 (531)	Reference		
7yrs	99.4 (62420)	0.6 (352)	1.14	0.96 - 1.36	0.1342
8yrs	99.3 (61626)	0.7 (434)	1.42	1.19 - 1.68	<0.0001
9yrs	98.7 (60323)	1.3 (822)	2.75	2.31 - 3.28	<0.0001
10yrs	97.2 (50577)	2.8 (1463)	6.05	5.05 - 7.25	<0.0001
11yrs	95.4 (48982)	4.6 (2373)	10.32	8.94 - 11.92	<0.0001
12yrs	92.4 (38380)	7.6 (3150)	17.95	15.68 - 20.56	<0.0001
13yrs	88.1 (35708)	11.9 (4834)	29.52	25.82 - 33.75	<0.0001
14yrs	83.3 (27997)	16.7 (5627)	44.43	38.91 - 50.74	<0.0001
Time for Playing and Entertainment (Hours per day)	1.79 ± 0.94 *	1.54 ± 0.88 *	0.90	0.88 - 0.93	<0.0001
Gender					
Male	96.5 (262805)	3.5 (9444)	Reference		
Female	95.8 (232753)	4.2 (10142)	1.16	1.12 - 1.2	<0.0001
Parental_myopia					
Neither	97.0 (313178)	3.0 (9604)	Reference		
Either	95.4 (102226)	4.6 (4974)	1.72	1.59 - 1.86	<0.0001
Both	94.1 (80154)	5.9 (5008)	2.62	2.4 - 2.87	<0.0001

Birth Time of the year					
Before September 1st	96.1 (326545)	3.9 (13418)	Reference		
After September 1st	96.5 (169013)	3.5 (6168)	0.77	0.75 - 0.8	<0.0001
Rest after Continuous Use of Eye					
Never	95.6 (108908)	4.4 (4956)	Reference		
Sometimes	96.1 (285151)	3.9 (11604)	0.97	0.93 - 1.01	0.1275
Usually	97.1 (101499)	2.9 (3026)	0.85	0.81 - 0.9	<0.0001
Too Close to Book While Reading					
Never	96.8 (94796)	3.2 (3145)	Reference		
Sometimes	96.5 (284773)	3.5 (10391)	1.22	1.16 - 1.27	<0.0001
Usually	95.0 (115989)	5.0 (6050)	1.58	1.5 - 1.67	<0.0001
Too Close to Television While Watching					
Never	96.3 (176834)	3.7 (6745)	Reference		
Sometimes	96.3 (251251)	3.7 (9775)	1.07	1.03 - 1.11	0.0002
Usually	95.7 (67473)	4.3 (3066)	1.06	1 - 1.12	0.0460

CI = Confidence Interval

*mean ± SD

High Myopia is defined as: Non Cyclo Sphere Equivalent <= (-5D)

Logistic Regression with Robust Estimation of Variance was used to count for correlation within cluster

AUC = 0.833

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation
√Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found
Introduction		
√Background/rationale	2	Explain the scientific background and rationale for the investigation being reported
√Objectives	3	State specific objectives, including any prespecified hypotheses
Methods		
√Study design	4	Present key elements of study design early in the paper
√Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection
√Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants
√Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable
√Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group
√Bias	9	Describe any efforts to address potential sources of bias
√Study size	10	Explain how the study size was arrived at
√Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why
√Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding
		(*b*) Describe any methods used to examine subgroups and interactions
		(*c*) Explain how missing data were addressed
		(*d*) If applicable, describe analytical methods taking account of sampling strategy
		(*e*) Describe any sensitivity analyses
Results		
√Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed
		(b) Give reasons for non-participation at each stage
		(c) Consider use of a flow diagram
√Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders
		(b) Indicate number of participants with missing data for each variable of interest
√Outcome data	15*	Report numbers of outcome events or summary measures
√Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included
		(*b*) Report category boundaries when continuous variables were categorized
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period
√Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses

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Discussion		
√Key results	18	Summarise key results with reference to study objectives
√Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias
√Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence
√Generalisability	21	Discuss the generalisability (external validity) of the study results
Other information		
√Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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